REMARKS

The specification has been amended to set forth the SEQ ID NOs of the sequences shown in Figures 7 and 8.

A substitute Sequence Listing has been provided to include SEQ ID NOs:19 and 20 which are sequences shown in Figure 7. A computer readable form of the substitute Sequence Listing is submitted with a Statement Pursuant to 37 C.F.R. § 1.821(f). No new matter is introduced by this substitute Sequence Listing.

Claim 1 has been amended to restrict the modification to the substitution of Cys for Trp at position 258 based on the amino acid numbering of the rice protein. Claim 1 has been further amended to remove the objected language. Claims 5, 6, 10, 11, 12, 15 and 16 have been amended to remove the rice nucleic acid claimed in the parent application. Claim 10 has further been amended to add "sorghum nucleic acid" which had inadvertently been dropped in the copy of the claims submitted with the previous amendment. Claim 22 has been amended to delete the objected language. Claims 2, 8 and 13 have been canceled.

It is submitted that none of these amendments constitute new matter, and their entry is requested.

The specification has been amended to set forth the SEQ ID NOs of Figures 7 and 8. It is submitted that this amendment places the application in compliance with the Sequence Rules.

The cancellation of claims 2, 8 and 13 obviates the objection to the claims.

Claims 1, 6, 11, 16 and 22 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite. It is submitted that the amendments to the claims obviate this rejection. Withdrawal of this rejection is requested.

Claims 1, 2, 5-8, 10-13, 15-19 and 20-22 were rejected under 35 U.S.C. §112, first paragraph, for lack of written description. It is submitted that restriction of the claims to the substitution of Cys for Trp at residue 258 based on the amino acid numbering of the rice protein obviates this rejection. Withdrawal of this rejection is requested.

Claims 1, 2, 5-8, 10-13, 15-19 and 20-22 were rejected under 35 U.S.C. §112, first paragraph for lack of enablement with respect to any modification of the L3 protein. It is submitted that

restriction of the claims to the substitution of Cys for Trp at residue 258 based on the amino acid numbering of the rice protein obviates this rejection. Withdrawal of this rejection is requested.

Claims 1, 2, 5-8, 10-13, 15-19 and 20-21 were rejected under 35 U.S.C. §103(a) as being unpatentable over Kim et al. (1990) in view of Schultz et al. (1983) and in further view of Kim et al. (1991) and Bohn et al. (1997). In response to this rejection, Applicants are filing Rule 131 Declarations by Linda J. Harris and Steve Gleddie swearing behind the Bohn et al. reference. Since Bohn et al. is no longer prior art in view of these Rule 131 Declarations, it is submitted that the rejection must fail.

Specifically, as noted in Applicants' previous response, Kim et al. (1990) describes two plant RPL3 genes from the dicot plant *Arabidopsis thaliana.* A section of the yeast L3 gene was used as a probe to identify the corresponding *A. thaliana* genes. The difference between the yeast sequence tcm1 and the two *Arabidopsis* sequences is shown in Figure 3 of Kim et al. (1990). For the Examiner's convenience, the sequence comparison (see the enclosed Figure) was reproduced, comparing each of the *Arabidopsis* sequences (M32654 and M32655) with the protein encoded by the yeast tcm1 gene (Z74971). As the Examiner will note, there are many differences in amino acid structure between these two genes. Each of the *Arabidopsis* genes, ARP1 and ARP2, contain about 140 amino acid changes. The amino acid sequence shown in Figure 3 of Kim et al. (1990) is taken from Schultz et al. (1983). There is no indication in these two references, taken alone or together, as to what amino acid change(s) is responsible for the trichodermin resistance noted in yeast containing this gene.

Kim (1991) states, as an objective, to characterize the steady-state RNA levels of two cloned L3 encoding genes developmentally; to compare tissue-specificity of these genes at the RNA level; to isolate trichothecene-resistant mutants in *Arabidopsis*; and to genetically characterize these mutants. The Abstract states that eight trichodermin- and T-2 toxin-resistant mutant plants were isolated. However, there is no characterization of the mutant plants and there is no sequence information provided which would indicate what mutations were responsible for the trichodermin- and T-2 toxin-resistant mutant plants.

As noted previously, the prior art does not provide any guidance as to what is the important change in these genes, which results in trichodermin resistance. The Kim et al. (1990) paper provides the sequence information for two corresponding genes in *Arabidopsis* and their later abstract publication (1991) suggest that they may have isolated mutant plants. However, no information is provided as to what was the cause of the mutation. As noted previously, even if one were to know what amino acid had been altered in the yeast tcm1 coding sequence, it was not obvious that the same modification in the plant RPl3 protein would function properly in plants. The protein RPL3 is one of approximately 70 plant ribosomal proteins. How these proteins are assembled, how they interact with each other and with ribosomal RNA, and what residues are essential for ribosomal activity are not known in plants and certainly cannot be predicted from the sequence data in Kim et al. (1990) or Schultz et al. The critical modification is within a highly conserved region (sorghum, wheat, corn, rice and barley encoded RPL3 proteins which are 100% identical from amino acid positions 209-284), and it is not obvious that, if one makes a change in this region, the protein would still function properly within the plant ribosomal complex.

The expression/production of ribosomal genes/proteins in ribosomal assembly in mammals and lower eukaryotes such as yeast have been shown to be stringently regulated, e.g., by rapid degradation of excess protein. Much less is known about how ribosomal genes and proteins are regulated and assembled in plants. There is no prior research demonstrating that one can modify a ribosomal protein gene, reintroduce it into a plant with a constitutive promoter, and have it function properly. Applicants demonstrated by tobacco transformation that the modified Rpl3 gene functioned in plants. This necessitated conducting site-specific mutagenesis on the rice Rpl3 cDNA, inserting the sequence into an *Agrobacterium* vector, and transforming tobacco plants. Since tobacco is not a host of *Fusarium graminearum*, Applicants needed to develop assays to test the direct effect of trichothecene mycotoxins on transformed tobacco cells and did so with cell suspension cultures as well as protoplants. It was not sufficient to introduce the unmodified version of the rice Rpl3 gene – this did not confer any DON tolerance to the transgenic plant cells and protoplasts – it was the modification which was important to provide trichothecene tolerance. It

could not be easily predicted that one could use information from a chemical tolerance mutant screen in yeast to produce a transgenic plant tolerant for a broad host fungal pathogen.

Therefore, Applicants respectfully submit that the claims as now amended are patentable over Kim et al. (1990) in view of Schultz et al. (1983) and Kim (1991). As noted above, the reference of Bohn et al. (1997) is not prior art in view of the Rule 131 Declarations filed concurrently herewith.

In view of the amendments to the claims and the above remarks, it is submitted that the cited prior art does not render the claimed subject matter obvious. Withdrawal of this rejection is requested.

In view of the above amendments and remarks, it is submitted that the present claims satisfy the requirements of the patent statutes and are patentable over the prior art. Reconsideration and early notice of allowance are requested. The Examiner is invited to telephone the undersigned in order to expedite prosecution of the present application.

RESPECTFULLY SUBMITTED,			
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